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ANNUAL RESEARCH PROGRESS REPORT

FY 1997

Grand Forks Human Nutrition Research Center

GRAND FORKS
HUMAN NUTRITION
RESEARCH CENTER
U.S. DEPARTMENT OF
Agriculture

ANNUAL RESEARCH PROGRESS REPORT

(FY 1997)

GRAND FORKS HUMAN NUTRITION RESEARCH CENTER

**UNITED STATES DEPARTMENT OF AGRICULTURE
AGRICULTURAL RESEARCH SERVICE
NORTHERN PLAINS AREA**

GRAND FORKS, NORTH DAKOTA 58202

MINERAL NUTRIENT REQUIREMENTS

MANAGEMENT UNIT

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0149753 Year: 97 Project Number: 5450-51000-012-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.1.3.4 50%

Title: EFFECTS OF COPPER DEPLETION ON CARDIOVASCULAR
FUNCTION AND METABOLISM

Period Covered From: 03/96 To: 03/01

Progress Report:

Nephropathy is the most serious cause of disability and death among people with diabetes mellitus. Transgenic mice with an overexpression of the calmodulin gene developed abnormal kidney anatomy along with insulin resistance, hyperglycemia, and increased urea nitrogen in blood. Surprisingly, urinary protein was not markedly increased. These mice will be useful in studying nutritional factors such as copper and chromium that can modify the diabetic process. When dietary copper is marginal, but not very deficient, excess dietary iron can cause increased plasma cholesterol. People with iron overload may benefit from a copper supplement. The early nutritional work on copper deficiency and human pellagra were reviewed and put into a modern context as a guide for scientists attempting to prevent important modern illnesses by nutritional means. Copper deficiency in rats increases vascular superoxide, which, in turn, decreases arterial relaxation mediated by nitric oxide. Impaired vascular relaxation may explain hypertension in deficient rats and may contribute to high blood pressure in people. Copper deficiency also decreases the amount of dehydroepiandrosterone (DHEA) in serum. DHEA is thought to decrease both risk of heart disease in men and some of the adverse changes associated with the aging process. A diet based on unrefined plant food and high in whole grains, olive oil, nuts, sesame seeds, green tea, etc., fed to women was less of an oxidative damage hazard than a typical Western diet containing the same amount of fat. The need for protection by dietary copper and selenium against oxidative damage was decreased as was oxidation of plasma cholesterol. Cholesterol oxidation may contribute to human heart disease. An intake of magnesium close to the Recommended Dietary Allowance (RDA) induced less cardiac irritability in women than a similar diet containing 100 mg/day. Cardiac function was assessed with 20 hr electrocardiograms. This is the first physiological evidence in support of the magnesium RDA. Multiple trace elements were measured in the scalp hair collected over two decades from one man to better define the usefulness of this method in clinical and experimental medicine. Coefficients of variation ranged from 11% for zinc to 150% for potassium; inferences about health from a single analysis of hair probably are invalid. Ouabain, an inhibitor of cardiac ATPase, induced cardiac arrhythmias in copper deficient rats. These data are useful to committees who establish RDAs and to people who plan human diets and plan research, as the U.S. diet often is low in copper.

Publications:

01. CARLSON, E.C., AUDETTE, J.L., KLEVAY, L.M., NGUYEN, H. and EPSTEIN, P.N. 1997. Ultrastructural and functional analyses of nephropathy in calmodulin-induced diabetic transgenic mice. Anat. Rec. 247: 9-19.

Approved: FORREST H NIELSEN
Title: CENTER DIRECTOR

Date: 01/98

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FUNCTION AND METABOLISM

Period Covered From: 03/96 To: 03/01

Publications: (Continued)

02. KLEVAY, L.M. 1997. Iron can be cholesterotropic and cuprotropic. 9th Intl. Symp. on Trace Elements in Man and Animals, P.W.F. Fischer, M.R. L'Abbe, K.A. Cockell and R.S. Gibson, eds, NRC Res. Press, Ottawa, pp 614-615.
03. KLEVAY, L.M. and OLSON, R.E. 1997. Pellagra is not infectious! (Goldberger, 1916). J. Nutr. 127: 1032S-1034S.
04. KLEVAY, L.M. 1997. Copper as a supplement to iron for hemoglobin building in the rat. J. Nutr. 127: 1034S-1036S.
05. KLEVAY, L.M. 1997. And so spake Goldberger in 1916: pellagra is not infectious. J. Am. Coll. Nutr. 16: 290-292.
06. LYNCH, S.M., FREI, B., MORROW, et.al. 1997. Vascular superoxide dismutase deficiency impairs endothelial vasodilator function through...and increased lipid peroxidation. Arterioscler. Thromb. Vasc. Biol. 17: 2975-2981.
07. KLEVAY, L.M. and CHRISTOPHERSON, D.M. 1997. Copper deficiency decreases dehydroepiandrosterone (DHEA) in rat serum. FASEB J. 11: A183.
08. SPILLER, G.A., KUYPERS, F.A., BRUCE, B., ROITMANS, E. and KLEVAY, L. 1997. Diets high in phytochemicals and fiber decrease plasma cholesterol oxidation. Am. J. Clin. Nutr. 66: 207.
09. KLEVAY, L.M., JOHNSON, L.K., MILNE, D.B. and NIELSEN, F.H. 1997. Dietary magnesium near the RDA yields less ectopy on Holter cardiograms than 100 mg daily. Am. J. Clin. Nutr. 66: 49.
10. SPILLER, G.A., BRUCE, B., KLEVAY, L.M. and GALLAGHER, S.K. 1997. Diets high in phytochemicals and fiber may decrease the need for intrinsic defense against oxidative damage. FASEB J. 11: A585.

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ANNUAL RESEARCH PROGRESS REPORT
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FUNCTION AND METABOLISM

Period Covered From: 03/96 To: 03/01

Publications: (Continued)

11. CHRISTOPHERSON, D., SHULER, T.R. and KLEVAY, L. M. 1997. Multiple trace elements in hair of one man over two decades: methodology. ND Acad. Sci. 51: 185.
12. MCLEAN, S.A., ONWOCHEI, M.O., ASKARI, A. and KLEVAY, L.M. 1997. Copper deficiency enhances the toxicity of ouabain to hearts perfused by the Langendorff method. FASEB J. 11: A362.

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Date: 01/98

Title: CENTER DIRECTOR



ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0400377 Year: 97 Project Number: 5450-51000-020-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.2 60% 5.1.3.3 40%Title: HOMEOSTASIS AND BIOAVAILABILITY OF TRACE ELEMENTS
IN HUMANS AND ANIMALS

Period Covered From: 04/96 To: 04/01

Publications: (Continued)

04. MARENTES, E., SHELP, B.J., VANDERPOOL, R.A. and SPIERS, G.A. 1997. Retranslocation of boron in broccoli and lupin during early reproductive growth. *Physiol. Plant.* 100: 389-399.

05. FINLEY, J.W. and JOHNSON, L.K. 1997. Dietary manganese and serum ferritin concentration affect manganese absorption and retention. *FASEB J.* 11:A148.

Approved: FORREST H NIELSEN
Title: CENTER DIRECTOR

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0400398 Year: 97 Project Number: 5450-51000-021-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.2 60% 5.1.3.3 40%Title: BIOAVAILABILITY OF TRACE ELEMENTS, ESPECIALLY IRON
FROM FOOD, & ITS INFLUENCE ON NUTRITUDE & FUNCTION

Period Covered From: 04/96 To: 03/01

Progress Report:

The ability of humans to adapt to dietary iron (Fe) bioavailability was evaluated by measuring iron absorption in men before and after consuming diets that enhance or inhibit iron absorption (diets with high or low iron bioavailability). Healthy men were randomly assigned to consume 1 of 2 weighed diets for 12 wk. The high bioavailability diet provided refined grain products, no coffee or tea, and ample meat, poultry and ascorbic acid. The low bioavailability diet contained no meat, limited poultry or fish, considerable legume and whole grain products, tea at each meal, and just adequate ascorbic acid. The high and low bioavailability diets contained, respectively, 16.2 and 16.6 mg nonheme iron and 2.0 and 0.1 mg heme iron daily per 3500 kcal. Heme and nonheme iron absorption from the entire 2-d menu were measured with radiotracers at 0 and 10 wk, by using whole body scintillation counting and the ratio of Fe-55/Fe-59 in blood. Preliminary data from 19 men indicated a 25 ug/L decrease in serum ferritin between wk 0 and 12, independent of diet. Despite this, nonheme iron absorption decreased 40% with the high bioavailability diet after 10 wk. Nonheme iron absorption increased 30% with the low bioavailability diet (significantly different absorption ratios at 10/0 wk). This partial adaptation changed the relative nonheme iron bioavailability between the two diets from 5-fold (high bioavailability 3.7 vs low 0.7%, p<0.01 at 0 wk) to just over 2-fold (2.2 vs 0.9%, p<0.01 at 10 wk). Heme iron absorption did not adapt. These data indicate that biological adaptation reduces the influence of dietary iron bioavailability with time. They also suggest that adult men's absorptive efficiency is not minimized, but can be reduced or enhanced to return toward an original "set-point". Although a cross-sectional inverse relationship between serum ferritin and nonheme iron absorption is well established, these results demonstrate, for the first time, a longitudinal adaptation in iron absorption, apparently independent of serum ferritin. An additional study has begun to determine the influence of iron supplementation on adaptation in iron absorption by adult men and women consuming a beef meal. These studies will help define dietary advice to consumers concerning iron nutrition. The effects of varying amounts of dietary iron, copper (Cu), and zinc (Zn) on indices of iron status and oxidative stress were studied in an experiment with rats. In this experiment, iron status was primarily affected by dietary iron and was slightly influenced by dietary zinc and copper. High dietary iron did not induce overt oxidative stress, as measured by liver and heart TBARS (thiobarbituric acid-reactant substances) and vitamin E. Dietary copper primarily influenced the animal's antioxidant capacity (increased liver and heart superoxide dismutase and serum ceruloplasmin) with some modification by dietary Fe and Zn. The results suggest that dietary Cu, Fe, and Zn interact to influence some portions of the body's oxidative defense system.



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FROM FOOD, & ITS INFLUENCE ON NUTRITION & FUNCTION

Period Covered From: 04/96 To: 03/01

Publications:

01. HUNT, J.R. and PENLAND, J.G. 1997. Impaired startle response in growing rats marginally iron-depleted without overt anemia. In: Trace Elements in Man and Animals - TEMA 9, Banff, Alberta, Canada, pp. 220-221.
02. HUNT, J.R. and ZITO, C.A. 1997. Serotonin uptake by blood platelets of rats is reduced in severe but not marginal dietary iron deficiency. Proc. ND Acad. Sci. 51:201.
03. HUNT, J.R. 1997. Do common sources of dietary protein increase calcium needs? J. Am. Dietet. Assoc. 97:1370.
04. ROUGHEAD, Z.K. and HUNT, J.R. 1997. Dietary iron bioavailability affects fecal ferritin content in women consuming vegetarian and non-vegetarian diets. FASEB J. 11:A443.
05. HUNT, J.R. and ZITO, C.A. 1997. Severe, but not marginal dietary iron deficiency reduces serotonin uptake into blood platelets of rats. FASEB J. 11:A570.
06. HUNT, J.R. and ROUGHEAD, Z.K. 1997. A lacto-ovo-vegetarian diet for 8 weeks decreased iron absorption and fecal ferritin excretion without affecting blood indices...premenopausal women. Intl Symp on Fe in Biol and Med p 289.
07. HUNT, J.R. 1997. Reduced urinary calcium on a vegetarian diet may reflect reduced calcium absorption with phytic acid, not calcium conservation with less meat protein. J. Am. Dietet. Assoc. 97:A19.

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Title: CENTER DIRECTOR

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0147555 Year: 97 Project Number: 5450-51000-021-02 S
Mode Code: 5450-10-00 STP Codes: 5.1.3.2 60% 5.1.3.3 40%

Title: IMPROVEMENT OF WHOLE BODY COUNTING EQUIPMENT AND
METHODS FOR MINERAL ELEMENT METABOLIC STUDIES

Period Covered From: 01/97 To: 12/97

Progress Report:

Whole body counting measurements were conducted to support human studies investigating the absorption of dietary copper in persons with cardiovascular disease, and the effect of dietary iron bioavailability on biological adaptation in iron absorption. After flood damage to the research center, the human whole body counter and radioactive meal counter were fully restored. Preliminary analysis of data from "extra" detectors for measuring radioactivity at specific organ sites indicated a need to increase detector sensitivity. Pilot work with cadmium-115 m indicated that use of this short-lived isotope is not practical, and that further such work should use cadmium-109. The detectors of the flood-damaged small animal whole body counter were commercially refurbished, and the data acquisition and processing system/programs re-designed. The work is nearly completed, and the small animal counter is expected to be fully operational in January, 1998.

Publications:

01. MOMCILLOVIC, B. and LYKKEN, G.I. 1997. Non-invasive in vivo assessment of 54Mn kinetics in the brain and liver of obese premenopausal women. FASEB J. 11:A594.
02. ALKHATIB, H.A., DUEURRE, J.A., LONG, W.M., FREY, W.H., MOMCILLOVIC, B. and LYKKEN, G.I. 1997. 210Po...in the brain protein fractions in Alzheimer's disease and in the lipid fraction in Parkinson's Disease. FASEB J. 11:A631.
03. MOMCILLOVIC, B., ALKHATIB, H.A., DUEURRE, J.A., COOLEY, M., HARRIS, T.R. and LYKKEN, G.I. 1997. What do radon daughters...transport. Proc 17th Workshop on Macro & Trace Elem. Freidrich-Schiller-Univ. 84t Jena, pp. 574-88, Dec.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0401160 Year: 97 Project Number: 5450-51000-021-03 T
Mode Code: 5450-10-00 STP Codes: 5.1.3.2 60% 5.1.3.3 40%

Title: ADAPTATION IN THE ABSORPTION OF IRON FROM BEEF

Period Covered From: 10/97 To: 12/97

Progress Report:

The overall goal of this new project is to determine whether people biologically adapt their absorption of heme and nonheme iron from a meat-based meal in response to previous iron intake. Specifically, it will be determined a) whether heme iron absorption from a meat-based meal is reduced after iron supplementation, b) whether nonheme iron absorption from a meat-based meal is reduced after iron supplementation, c) whether intestinal ferritin production, as measured in fecal samples, is increased after iron supplementation, and is associated with changes in heme and nonheme iron absorption, and d) whether serum ferritin is increased substantially after iron supplementation, and if any increase in serum ferritin persists after iron supplementation is discontinued. The experiment was designed, approved by institutional review committeeess for use with human subjects, and partial funding was obtained from the National Cattlemen's Beef Association. Volunteer enrollment began at the first of November, and 13 volunteers had been enrolled in the study by the end of 1997.

Publications:

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0400524 Year: 97 Project Number: 5450-51000-022-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.1.3.4 50%Title: HUMAN MINERAL ELEMENT REQUIREMENTS AND THEIR
MODIFICATION BY STRESSORS

Period Covered From: 05/96 To: 05/01

Progress Report:

An experiment performed with men between the ages of 22 and 40 years housed in a metabolic ward showed that dietary fructose and magnesium affect macromineral metabolism. Eleven men participated in four dietary periods of 42 days in which dietary magnesium was either approximately 170 or 370 mg/day, and dietary fructose was either 4% or 19% of energy. A decaffeinated carbonated beverage containing high fructose corn syrup replaced cornstarch, bread and rice in the low fructose diet to give the high fructose diet. The protein from the high starch foods was replaced by egg white protein. The treatments were randomized so that 2 to 3 individuals were on each treatment during each 42 day period. With the low fructose diet (high starch), when dietary magnesium was about 170 mg/day, magnesium balance was -14 mg/day; because this value was markedly lower than when dietary magnesium was 370 mg/day (29 mg/day), an intake of 170 mg/day is probably inadequate for men consuming a high starch diet. Feeding high fructose increased magnesium balance, but it also decreased calcium balance with the effect more marked when dietary magnesium was low. High dietary fructose also decreased phosphorus balance and increased the concentration of alkaline phosphatase in plasma. These findings will be useful to those involved in setting nutritional guidelines for magnesium and in establishing the effect of high fructose intakes on mineral metabolism.

Publications:

01. NIELSEN, F.H. 1996. Controversial chromium. Does the superstar mineral of the mountebanks receive appropriate attention from clinicians and nutritionists? *Nutr. Today* 31:226-233.
02. NIELSEN, F.H. 1997. Beyond copper...and zinc: Other elements that will be found important by the year 2000. IN: P.W.F. Fischer, et al (eds). 9th Int. Symp. Trace Elem. in Man & Animals, NRC Res. Press, Ottawa, pp 653-55.
03. NIELSEN, F.H. 1996. Evidence for the nutritional essentiality of boron. *J. Trace Elem. Exp. Med.* 9:215-229.
04. NIELSEN, F.H. and MILNE, D.B. 1997. Dietary fructose and magnesium effect macromineral metabolism in men. *Proc. N.D. Acad. Sci.* 51:212.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0400524 Year: 97 Project Number: 5450-51000-022-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.1.3.4 50%Title: HUMAN MINERAL ELEMENT REQUIREMENTS AND THEIR
MODIFICATION BY STRESSORS

Period Covered From: 05/96 To: 05/01

Publications: (Continued)

05. NIELSEN, F.H. 1997. Boron in human and animal nutrition. Plant and Soil 193:199-208.

06. NIELSEN, F.H. 1997. Boron. IN: B.L. O'Dell and R.A. Sunde (eds) Handbook of Nutritionally Essential Mineral Elements, Marcel Dekker, New York, NY, pp. 453-464.

07. NIELSEN, F.H. 1997. Vanadium. IN: B.L. O'Dell and R.A. Sunde (eds), Handbook of Nutritionally Essential Mineral Elements, Marcel Dekker, New York, NY pp. 619-630.

08. NIELSEN, F.H. 1997. Nutritional and therapeutic implications of chromium. IN: J. Anderson, P. Kendall and C. Pineda (eds), Lillian Fountain Smith Conf. for Nutr. Educators 1997 Program Synopsis, Ft Collins, CO, pp 43-46.

09. NIELSEN, F.H. 1997. Nutrition, trace elements. IN. R. Dulbecco, (ed), Encyclopedia of Human Biology. 2nd Ed., Vol 6. Academic Press, San Diego, CA, pp. 373-383.

10. NIELSEN, F.H. 1996. Foreword for Workshop "New Approaches, Endpoints and Paradigms for RDAs of Mineral Elements." J. Nutr. 126:2299S.

11. NIELSEN, F.H. 1997. The justification...providing dietary guidance for the nutritional intake of boron. IN: Abstracts of 2nd Int. Symp. on the Health Effects of Boron and Its Compounds, Univ. California, Irvine, CA, p. 49.

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Date: 01/98

Title: CENTER DIRECTOR



ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0400048 Year: 97 Project Number: 5450-51000-022-02 T
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.3.1.2 50%Title: NEW METHODS OF ASSESSMENT OF SPECIFIC SUBOPTIMAL
MINERAL NUTRIENT STATUS IN HUMANS

Period Covered From: 01/97 To: 12/97

Progress Report:

Samples from 12 postmenopausal women, who had completed a metabolic study to investigate the effects of low and moderately high zinc intakes on copper and iron nutriture were analyzed. Volunteers were fed a mixed Western diet that supplied either 1 or 3 mg copper/day for two 90-day periods. During the first 90-day period, all of the subjects received 3 mg zinc/day and during the second 90-day period, all of the subjects received 53 mg zinc/day. High dietary zinc significantly increased extracellular superoxide dismutase activity among all of the subjects from 26.13 U/ml plasma at the end of the low dietary zinc period to 32.57 U/ml plasma at the end of the high dietary zinc period. There was no significant effect of dietary copper on extracellular superoxide dismutase activity. In contrast, erythrocyte copper-zinc superoxide dismutase activity was not significantly affected by dietary zinc. However, low dietary copper significantly depressed copper-zinc superoxide dismutase activity. High dietary zinc significantly depressed enzymatic ceruloplasmin activity, glycosylated hemoglobin concentrations, plasma copper concentrations, and ionized magnesium concentrations. High dietary zinc significantly increased plasma zinc concentrations and the percent platelet aggregation. These results suggest that 53 mg zinc/day has some adverse effects on copper metabolism. These results also suggest that measurements of extracellular superoxide dismutase activity may be a useful indicator of zinc status in humans. Human epidemiological studies indicate that selenium supplementation is associated with a reduction in cancer incidence. Animal studies were conducted to determine whether selenium supplementation would inhibit the formation of aberrant crypt foci, which are preneoplastic lesions observed in the colon following exposure to chemical carcinogens. The frequency of aberrant crypt foci were significantly decreased in animals supplemented with selenite or selenate but not selenomethionine. These results indicate that selenium, depending on chemical form, can be efficacious against chemically induced colon carcinogenesis. These findings will be useful to other scientists and to nutrition specialists providing guidance for intakes of mineral elements.

Publications:

01. DAVIS, C.D. 1997. Effect of dietary zinc and copper on Beta-amyloid precursor protein expression in the rat brain. J. Trace Elem. Exper. Med. 10:249-258.
02. DAVIS, C.D. and REEVES, P.G. 1997. Effect of dietary zinc and copper on Beta-amyloid precursor protein expression. FASEB J. A:183.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0400048 Year: 97 Project Number: 5450-51000-022-02 T
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 50% 5.3.1.2 50%Title: NEW METHODS OF ASSESSMENT OF SPECIFIC SUBOPTIMAL
MINERAL NUTRIENT STATUS IN HUMANS

Period Covered From: 01/97 To: 12/97

Publications: (Continued)

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Title: CENTER DIRECTOR



ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0149894 Year: 97 Project Number: 5450-51530-004-00 D
Mode Code: 5450-10-00 STP Codes: 5.1.3.3 25% 5.3.1.2 75%Title: DEVELOPMENT AND EVALUATION OF METHODS FOR THE
CLINICAL EVALUATION OF MINERAL NUTRITIONAL STATUS

Period Covered From: 05/96 To: 05/01

Progress Report:

Eleven men completed a study investigating the interaction between dietary fructose and dietary magnesium (Mg). High dietary fructose significantly ($P<0.01$) increased Mg balance during both low and high dietary Mg intakes. Ultrafilterable and ionized serum Mg were also affected by Mg and fructose intakes; they were higher when fructose was fed and when Mg intakes were high. High dietary fructose also depressed both calcium and phosphorus balances and increased urinary loss of phosphorus. These findings suggest that high dietary fructose adversely affects calcium and phosphorus metabolism in humans. Further studies are indicated to see if a high fructose diet coupled with low dietary Mg and marginal calcium leads to bone loss. A study with postmenopausal women is in progress to study the effects of dietary zinc (Zn) and copper (Cu) on indicators of Cu, Zn, and iron status. Half of the women are being fed a diet containing 1.0 mg Cu per day, the rest are being fed a diet containing 3.0 mg Cu per day. Both groups are receiving 3.0 mg of Zn per day for 90 days followed by 53 mg Zn per day for 90 days. Preliminary results from the first 12 women who have completed the study suggest that extracellular superoxide dismutase is directly related to Zn intake, but not to Cu intake. Conversely, erythrocyte superoxide dismutase is sensitive to Cu intake, but not Zn intake. High dietary Zn significantly depressed plasma Cu, ceruloplasmin, ionized Mg and glycosylated hemoglobin concentrations, and increased plasma Zn and percent platelet aggregation. These results suggest that 53 mg Zn per day has some adverse effects on Cu metabolism. The preceding is of use to other scientists and to individuals involved in determining the nutritional status of people.

Publications:

01. MILNE, D.B. 1997. Adult responses to various short-term dietary copper ... In: Trace Element Metabolism in Man and Animals-9, Fisher, P., L'Abbe, M., Cockell, K., Gibson, R., Eds, NRC Res. Press, Ottawa, pp 619-20.
02. MILNE, D.B. and NIELSEN, F.H. 1997. Dietary magnesium and copper affect indicators of copper and magnesium status in postmenopausal women. FASEB J. 11:A147.
03. MARCHELLO, M.J., HADLEY, M., SLANGER, W.D., MILNE, D.B. and DRISKELL, J.A. 1997. Nutrient composition of fed Bison. Proc 43rd Intl. Cong. Meat Science and Technology, pp 204-5.
04. GALLAGHER, S.K. and MILLER, S. 1997. Nutrition and the elderly. Advance Laboratory 6:45-50.

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ANNUAL RESEARCH PROGRESS REPORT
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CLINICAL EVALUATION OF MINERAL NUTRITIONAL STATUS

Period Covered From: 05/96 To: 05/01

Publications: (Continued)

05. GALLAGHER, S.K. 1997. Biochemical markers of bone metabolism as they relate
to osteoporosis. Med. Lab. Observer 29:50-59.Approved: FORREST H NIELSEN
Title: CENTER DIRECTOR

Date: 01/98

**MINERAL NUTRIENT FUNCTIONS
MANAGEMENT UNIT**

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0400186 Year: 97 Project Number: 5450-51000-018-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.1.3.4 25%Title: DIETARY TRACE ELEMENTS AND PHYSIOLOGY OF THE
CARDIOVASCULAR AND RELATED SYSTEMS

Period Covered From: 02/96 To: 02/01

Progress Report:

Long-term marginal copper deficiency in weanling male rats was found to enhance dilation of blood vessels early in the deficiency (1-2 months) and to impair dilation at later times (3-5 months); this illustrates that more than one event contributes to blood vessel alteration and that marginal copper deficiency leads to the same defect as severe deficiency when given enough time. Despite altered blood vessel dilation in copper-deficient rats, blood pressure was not affected; an apparent increase in excretion of sodium by the kidney may compensate for altered blood vessel function. Dilation of blood vessels in response to an inflammatory agent was greater in copper-deficient than in copper-adequate rats; by use of blocking agents, the pathway of this altered response was found to be related to enhanced release of histamine and prostaglandin metabolites. Studies of reduced blood clotting in copper-deficient rats provided further evidence that adhesion of platelets to blood vessel endothelial cells was reduced; reversal of the increased bleeding time by administration of von Willebrand factor illustrated the involvement of this clotting factor in the altered response. Mouse hearts in which the enzyme catalase was genetically over expressed were found to be protected against the oxidative stress of a simulated heart attack; this model may be used to study oxidative mechanisms in dietary copper deficiency. The first measurements of cardiac output in copper-deficient animals helped to show that, though cardiac output was not altered by copper deficiency, blood vessel resistance was reduced and volume of blood ejected per beat (stroke volume) of the heart was elevated; the higher stroke volume may contribute to the greater size of copper-deficient hearts. The first measurements of two important chemical messengers, nitric oxide and cyclic GMP, in copper-deficient hearts showed elevations in concentration that are consistent with their possible contribution to the reduction of heart force in copper deficiency. Adhesion of blood neutrophils to blood vessel walls, a necessary component of the immune response, was reduced by dietary copper deficiency. These findings should be useful for developing dietary recommendations for maintaining cardiovascular health.

Publications:

01. SAARI, J.T. 1996. Time-dependent alteration of relaxation of aortas from marginally copper-deficient rats. Med. Sci. Res. 24:727-729.
02. SCHUSCHKE, D.A., SAARI, J.T. and MILLER, F.N. 1997. Arteriolar dilation to endotoxin is increased in copper-deficient rats. Inflammation 21:45-53.

Approved: FORREST H NIELSEN
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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0400186 Year: 97 Project Number: 5450-51000-018-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.1.3.4 25%Title: DIETARY TRACE ELEMENTS AND PHYSIOLOGY OF THE
CARDIOVASCULAR AND RELATED SYSTEMS

Period Covered From: 02/96 To: 02/01

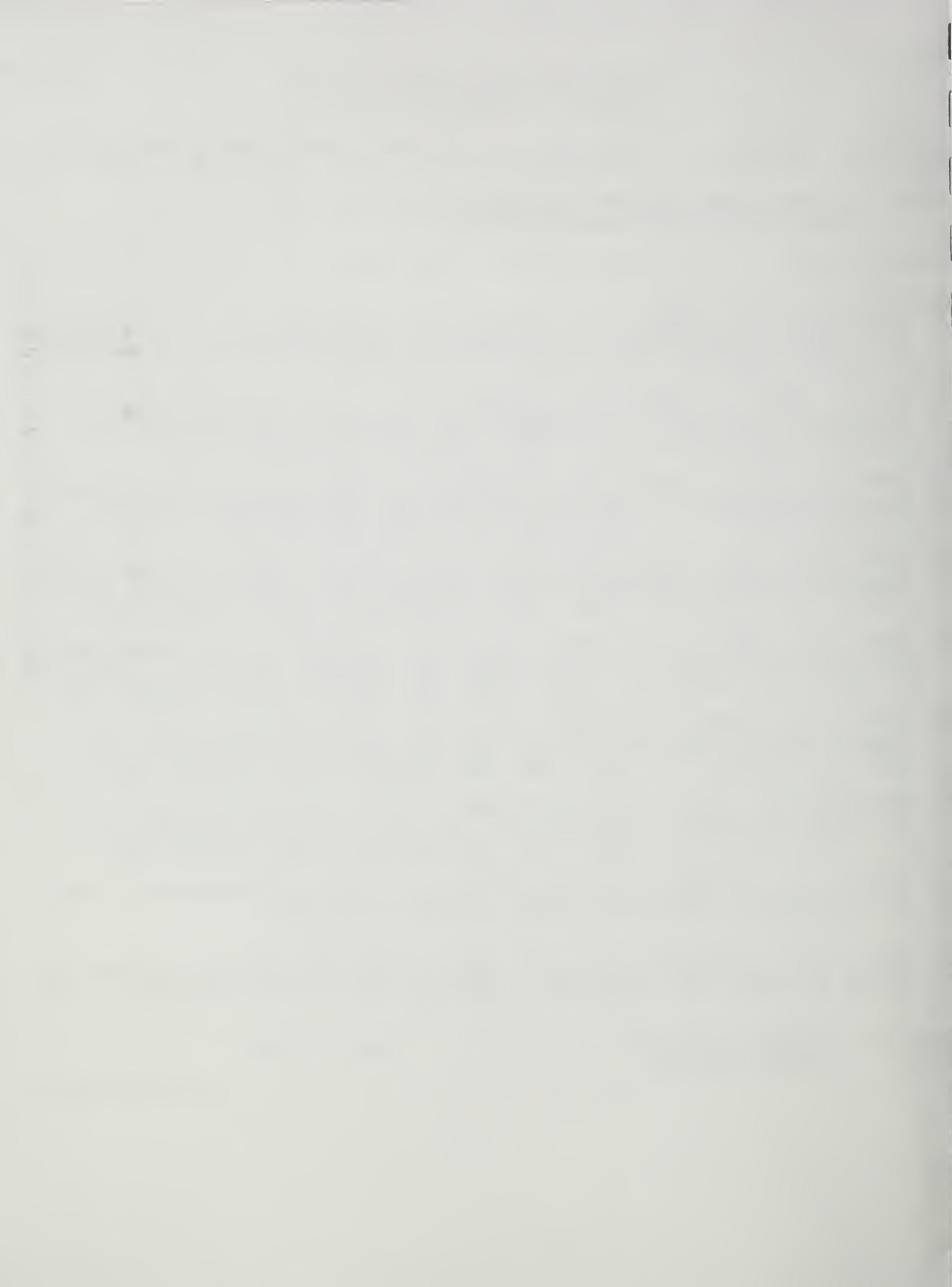
Publications: (Continued)

03. LOMINADZE, D.G., SAARI, J.T., MILLER, F.N., CATALFAMO, J.L. and SCHUSCHKE, D.A. 1997. Von Willebrand factor restores impaired platelet thrombogenesis in copper deficient rats. *J. Nutr.* 127:1320-1327.
04. LI, G., CHEN, Y., SAARI, J.T. and KANG, Y.J. 1997. Overexpression of catalase in the heart of transgenic mice increases its resistance to ischemia-reperfusion injury. *Am. J. Physiol.* 273:H1090-H1095.
05. CHEN, Y., YU, A., SAARI, J.T. and KANG, Y.J. 1997. Repression of hypoxia-hypoxia-reoxygenation injury in the catalase overexpressing heart of transgenic mice. *Proc. Soc. Exp. Biol. Med.* 216:112-116.
06. SAARI, J.T. 1997. Absence of hypertension in adult copper-deficient rats despite vascular...compensation, pp. 626-627. IN: P.W.F. Fischer, et al (ed.), *Proc. Ninth Int. Symp. TEMA*. NRC Research Press, Ottawa, Can.
07. KANG, Y.J., CHEN, Y. and SAARI, J.T. 1997. Transgenic mice overexpressing catalase specifically in...deficiency, pp. 337-339. IN: P.W.F. Fischer, et al (ed.), *Proc. Ninth Int. Symp. TEMA*. NRC Research Press, Ottawa, Can.
08. KANG, Y. J., CHEN, Y. and SAARI, J.T. 1997. Expression of...fed copper-deficient AIN-93G diet, pp. 377-79. IN: P.W.F. Fischer, et al (ed.) *Proc. Ninth Int. Symp. TEMA*. NRC Research Press, Ottawa, Can.
09. SCHUSCHKE, D., SAARI, J.T. and MILLER, F. 1997. Copper deficiency increases increases...endotoxin, pp. 242-243. IN: P.W.F. Fischer, et al (ed.) *Proc. Ninth Int. Symp. TEMA*. NRC Research Press, Ottawa, Can.
10. SAARI, J.T., STINNETT, H.O. and DAHLEN, G.M. 1997. Determinants of heart size in dietary copper deficiency. *FASEB J.* 11:A182.
11. SAARI, J.T. and DAHLEN, G.M. 1997. Nitric oxide and cGMP are elevated in hearts of copper-deficient rats. *16th Int. Cong. Nutr. Abstracts*, p. 256.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0400186 Year: 97 Project Number: 5450-51000-018-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.1.3.4 25%Title: DIETARY TRACE ELEMENTS AND PHYSIOLOGY OF THE
CARDIOVASCULAR AND RELATED SYSTEMS

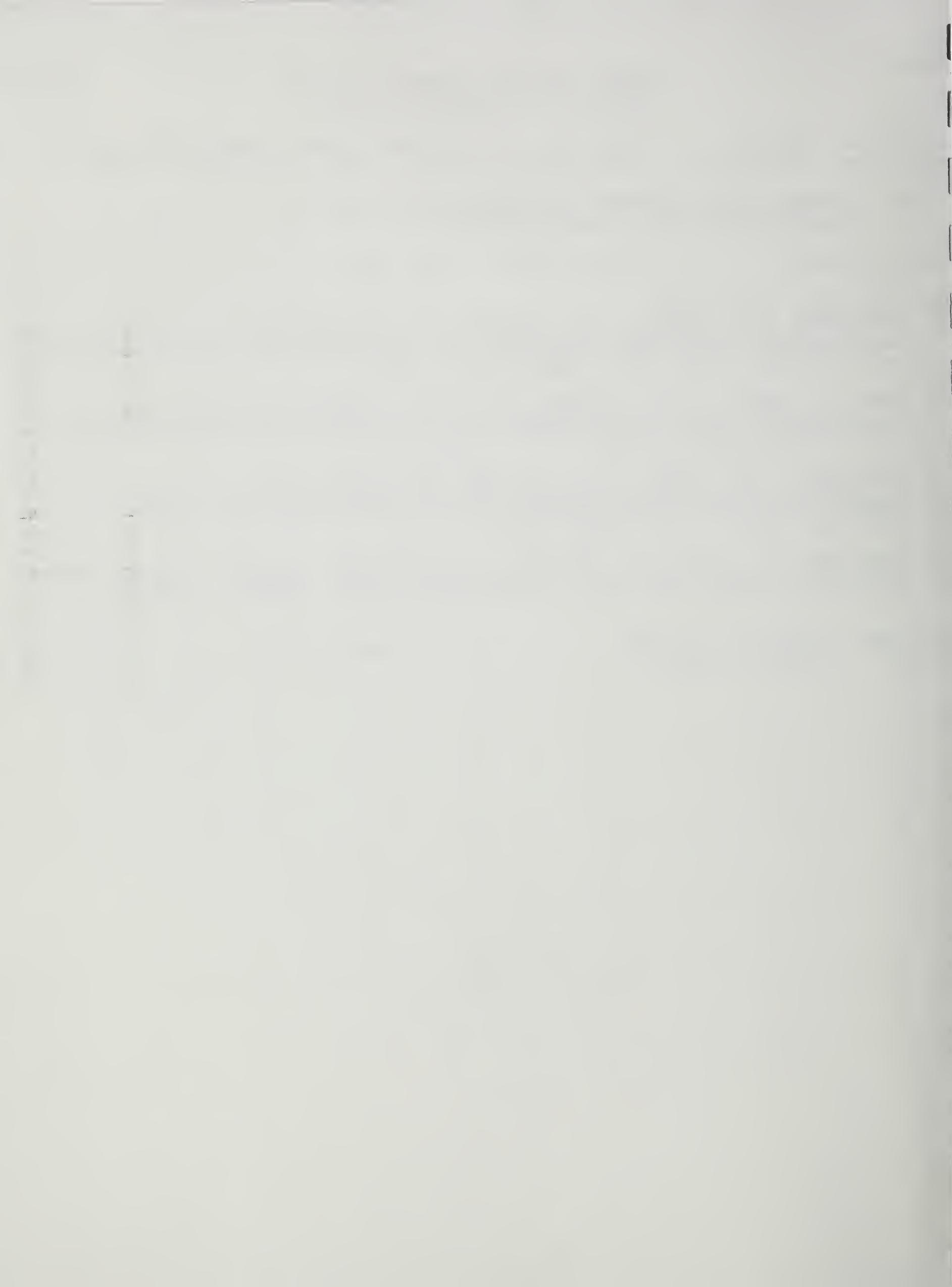
Period Covered From: 02/96 To: 02/01

Publications: (Continued)

12. SCHUSCHKE, D.A., SAARI, J.T., FALCONE, J.C. and MILLER, F.N. 1997. Dietary copper deficiency increases tone in resistance arterioles of the rat. 16th Int. Cong. Nutr. Abstracts, p. 255.
13. CHEN, Y., SAARI, J.T. and KANG, Y.J. 1997. Inhibition of hypoxia-reoxygenation injury in the heart of catalase overexpressing transgenic mice. Toxicologist 36:109.
14. ALEXANDER, J.M., SAARI, J.T. and KANG, Y.J. 1997. Alterations in expression of antioxidant enzymes in the heart of rats fed copper-deficient diet. Toxicologist 36:47.
15. SCHUSCHKE, D., SAARI, J., FLEMING, J. and MILLER, F. 1997. Dietary copper deficiency reduces neutrophil adherence in vivo. FASEB J. 11:A182.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0400106 Year: 97 Project Number: 5450-51000-019-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 90% 5.1.4.3 10%Title: MINERAL ELEMENT NUTRITION, NEUROPSYCHOLOGICAL
FUNCTION AND BEHAVIOR

Period Covered From: 03/96 To: 03/01

Progress Report:

Zinc (Zn) is essential for growth and early development, but the relationship between Zn and cognition in later development is unknown. A 2-year study in collaboration with the University of Texas Medical Branch and the Chinese Academy of Preventative Medicine found that Zn and micronutrient supplements improved cognitive and psychomotor function of rural and urban Chinese children, aged 6-9 years. Function was measured before and after 10 weeks of supplements containing 20 mg/d Zn and/or several other micronutrients at 50% recommended amounts. Motor skills, including manual dexterity and eye-hand coordination, visual perception, memory for simple shapes and complex objects, and reasoning were functions most improved by Zn and Zn combined with the micronutrients. Findings indicate that cognitive and psychomotor function, and thus school performance, may be suboptimal in the 6-10% of school-aged children in the United States who are Zn-deficient. Two other studies assessed the relationship of Zn nutriture and cognitive function in adults, but data analyses are not complete.

Manganese (Mn) is essential for normal brain function and behavior, and there has been speculation that moderate Mn excess or deficiency may be associated with an increase in aggressive behavior. Thirty-six male, Long-Evans rats (aged 90-100 days) were fed a diet containing 1, 10 or 100 ug Mn crossed with either 2500 or 5000 ug calcium (Ca) /g diet, for 12 weeks. A resident-intruder procedure was used to systematically assess and quantify aggressive, submissive and non-agonistic behaviors. Rats fed diets containing deficient or excessive concentrations of Mn were generally less active than those fed adequate Mn. Consequently, these rats engaged in fewer aggressive behaviors (attacking, biting, wrestling, aggressive contact) and displacement activities (exploration, self-grooming), and more posturing. However, rats fed diets high in Mn but low in Ca showed some increased aggressive behavior compared to rats fed other diets. Findings provide only weak support for earlier reports that Mn excess increases aggression. No support was found for the hypothesis that Mn deprivation is associated with increased aggression. Findings expand our knowledge of the functional role of dietary Mn, and its interaction with Ca, at physiological as well as toxicological concentrations.

Publications:

01. PENLAND, J.G., et al. 1997. A preliminary report: effects of zinc and micronutrient repletion on growth and neuropsychological function of urban Chinese children. *J. Am. College Nutr.* 16:268-272.
02. SANDSTEAD, H.H., PENLAND, J.G. and ALCOCK, N.W. 1997. Essentiality of zinc and...nutrition, pp. 109. IN: A.Langley, S. Mangas (eds.) Zinc. A Report Int. Mtg., Rundle Mall, Australia: So. Australian Hlth. Comm.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0400106 Year: 97 Project Number: 5450-51000-019-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 90% 5.1.4.3 10%Title: MINERAL ELEMENT NUTRITION, NEUROPSYCHOLOGICAL
FUNCTION AND BEHAVIOR

Period Covered From: 03/96 To: 03/01

Publications: (Continued)

03. HUNT, J.R. and PENLAND, J.G. 1997. Impaired startle response in growing rats marginally iron depleted...anemia, pp. 220-221. IN: P.W.F. Fischer et al (eds.) Proc. Ninth Int. Symp. TEMA. NRC Research Press, Ottawa, Can.
04. PENLAND, J.G. 1997. Trace elements, brain function and behavior: effects of zinc and boron, pp. 213-216. IN: P.W.F. Fischer et al (eds.) Proc. Ninth Int. Symp. TEMA. NRC Research Press, Ottawa, Can.
05. SANDSTEAD, H.H., ALCOCK, N.W., DAYAL, H., PENLAND, J.G. et al. 1997. Effects of zinc and...children, pp. 506-508. IN: P.W.F. Fischer et al (eds.) Proc. Ninth Int. Symp. TEMA. NRC Research Press, Ottawa, Can.
06. PENLAND, J.G. 1997. Moderate manganese excess and deprivation affects aggression responses of adult male rats. Proceedings of the Fifteenth International Neurotoxicology Conference.
07. PENLAND, J.G. 1997. The importance of boron for brain and psychological function. Proceedings of the Second International Symposium on the Health Effects of Boron and its Compounds, p. 47.

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Date: 01/98

Title: CENTER DIRECTOR

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0401450 Year: 97 Project Number: 5450-51000-023-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 80% 5.1.3.4 20%Title: BIOCHEMICAL CONSEQUENCES OF SUBOPTIMAL DIETARY
INTAKE OF TRACE ELEMENTS

Period Covered From: 04/97 To: 04/02

Progress Report:

Copper is essential to the development and function of the central nervous system. However, the biological role of copper in brain development and function is not entirely clear; factors other than copper's direct influence on the activities of copper-dependent enzymes may be involved. Adult female rats in three groups were fed diets containing two levels of low copper (1 and 2 ppm) and adequate copper (6 ppm) for a period beginning three weeks after parturition. Maternal diet containing 2 ppm copper reduced the rate of increase in protein kinase C gamma and diet containing 1 ppm copper reduced the rate of increase in protein kinase C alpha, beta and gamma in the brains of neonates. A subsequent experiment showed that low copper in maternal diets reduced protein kinase C alpha content in the hippocampus, protein kinase C beta content in the striatum, hypothalamus, hippocampus, and cerebral cortex, and protein kinase C gamma content in the striatum, medulla, hypothalamus, and cerebellum. Although protein kinase C does not contain copper, these data indicate that even moderate maternal copper deficiency may indirectly affect the expression of protein kinase C in specific regions of the developing neonatal brain. Because protein kinase C has an important regulatory role in the development of the central nervous system, these findings will help explain the biological role of copper in brain development and function and will be helpful in determining copper requirements during pregnancy and lactation for optimal brain development. Zinc status in humans and animals has a pronounced impact on reproduction and development in both sexes.

Angiotensin-I converting enzyme (ACE) in the testes serves a central role in the reproductive process of the male. ACE is a zinc-dependent enzyme and its activity is lost when animals are fed low-zinc diets. For the first time it was shown that the most likely reason for low ACE activity is that a zinc deficiency lowers the transcription rate of the ACE gene and, thus, the amount of ACE mRNA is reduced, which in turn, reduces the amount of ACE protein and activity. High concentrations of zinc in the diet can lower the copper status of humans and may eventually lead to signs of copper deficiency. This effect may be caused by zinc altering the transport of copper through the intestinal epithelial cell. To study this phenomenon, a cell culture system was devised that uses an intestinal cell mimic derived from a human colon carcinoma cell. High concentrations of zinc in the growth media inhibited copper transport. However, high zinc enhanced the uptake of copper into the cells. This work strongly suggests that zinc affects the activity of the two newly discovered copper transport proteins, Menkes and hCTR1, and for the first time, suggests a basic mechanism for the cause of low copper status in humans and animals fed high zinc diets.

Publications:

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0401450 Year: 97 Project Number: 5450-51000-023-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 80% 5.1.3.4 20%Title: BIOCHEMICAL CONSEQUENCES OF SUBOPTIMAL DIETARY
INTAKE OF TRACE ELEMENTS

Period Covered From: 04/97 To: 04/02

Publications: (Continued)

01. MOMCILLOVIC, B. and REEVES, P.G. 1997. Quantitative assessment of the effects of variability in dietary zinc dose-rate idiorhythms upon zinc deposition in bone of weanling rats...assay. *J. Nutr. Biochem.* 8:256-264.
02. MOMCILLOVIC, B., REEVES, P.G. and BLAKE, M.J. 1997. Idiorhythmic dose-rate variability in dietary zinc intake generates a different response pattern of zinc metabolism than conventional...feeding. *Br. J. Nutr.* 78:173-191.
03. JOHNSON, W.T., LABERGE, T.P. and SUKALSKI, K.A. 1997. Copper deficiency causes in vivo oxidative...rats, pp. 626-625. IN: P.W.F. Fischer, et al(ed.), *Proc. Ninth Int. Symp. TEMA*. NRC Research Press, Ottawa, Can.
04. JOHNSON, W.T. and THOMAS, A.C. 1997. Evidence of oxidative stress in HL60 cells deprived of copper. *FASEB J.* 11:A363.
05. JOHNSON, W.T. 1997. Book Review of *Handbook on Metals in Clinical and Analytical Chemistry*. *J. Am. Chem. Soc.* 117:1461.
06. DAVIS, C.D. and REEVES, P.G. 1997. Effect of dietary zinc and copper on beta-amyloid precursor protein expression. *FASEB J.* 11:A183.

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Date: 01/98

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0147990 Year: 97 Project Number: 5450-51000-023-03 T
Mode Code: 5450-20-00 STP Codes: 5.1.3.2 70% 5.2.2.2 30%Title: HEALTH EFFECTS AND BIOAVAILABILITY OF CADMIUM FROM
SUNFLOWER SEED KERNELS:A HUMAN STUDY

Period Covered From: 01/97 To: 12/97

Progress Report:

Cadmium (Cd) is a trace element that may be beneficial to some animals but if consumed in excess, it can cause kidney damage in humans. The confectionery sunflower plant takes up Cd from the soil and deposits it in the kernels. Studies were done to assess the availability and health effects of Cd from the kernels in human volunteers. These studies showed that individuals who reported consuming more than 1 ounce of kernels/wk over a long period were more likely to have higher Cd intake than those who ate less than one ounce/wk. However, no adverse health effects were found as a result of consuming these amounts of sunflower kernels. Other studies determined the absorption rate of Cd from sunflower kernels labeled with a stable isotope of Cd. Fresh ground labeled kernels were fed to 10 female volunteers as part of a single breakfast containing bread, jelly, milk and cereal. Over the following days, excreta were collected and the amount of labeled Cd was measured. The results showed that 11.4 +/- 2.4 percent of the stable isotope of Cd was absorbed. The range was 7.5 to 14.9 percent. This was somewhat higher than expected, because preliminary studies using radioactive Cd showed only 5 percent absorption by whole body counting techniques. Further research is ongoing to determine the long term effects of feeding a controlled amount of sunflower kernel Cd to human subjects. Information from these studies will be critical for consideration by the CODEX Alimentarius Commission, a United Nations Committee on Food Additives and Contaminants, when setting limits on the amount of Cd allowed in the imports of sunflower kernels, and for evaluating human lifetime body burden of Cd derived from dietary sources.

Publications:

01. REEVES, P.G. and VANDERPOOL, R.A. 1997. Cadmium burden of men and women who report regular consumption of confectionery sunflower kernels containing a natural...cadmium. Env. Health. Perspect. 105:1098-1104.

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Title: CENTER DIRECTOR

Date: 01/98

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0149978 Year: 97 Project Number: 5450-51520-011-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.2.2.2 25%Title: BIOCHEMICAL, PHYSIOLOGICAL, AND NUTRITIONAL ROLES
OF CERTAIN ULTRATRACE ELEMENTS

Period Covered From: 03/96 To: 03/01

Progress Report:

Findings obtained from experiments using rats indicate that boron is a natural food substance that allows bone to respond to the beneficial effects of moderate habitual exercise by modulating vitamin D metabolism. Normal amounts of boron in the diet increased the femur concentrations of calcium, phosphorus, and magnesium during a concurrent exercise regimen. Plasma 25-hydroxycholecalciferol concentrations were highest when rats received both exercise and normal amounts of boron. Collaborative work with scientists from Germany has shown that it is possible to use fuzzy logic for the derivation of nutrient requirements. Other novel mathematical approaches are also being developed for determining nutrient requirements. An initial nonlinear model has been set up to account for interactive effects of other nutrients and non-nutrients on requirements of a nutrient. These approaches are more objective than those used in the past and can be easily adapted to new information as it becomes available. Also, because they account for interactive effects (synergistic or antagonistic), the models can be tailored to a specific group of individuals. Findings were obtained showing that arsenic deprivation influences methionine metabolism in laboratory animals. Arsenic deprivation decreased liver concentrations of S-adenosylmethionine and the activity of betaine homocysteine methyltransferase. This information is being used by regulatory agencies involved in setting the limits of environmental arsenic exposure. Findings were obtained showing that physiological amounts of nickel interacts synergistically with folic acid, especially when folic acid is limiting in the diet. This is further circumstantial evidence that nickel has a physiological role in higher animals. An experiment with diabetes-prone and diabetes-resistant BB rats gave findings indicating that vanadium is a nutritionally important element involved in thyroid and glucose metabolism. Plasma thyroxine (T-4) concentrations were lower and triiodothyronine (T-3) concentrations were higher in vanadium-supplemented (0.5 ug/d diet) than vanadium-deficient (2 ng/g diet) fed deficient iodine (50 ng/g diet); luxuriant iodine (25 ug/g diet) changed the concentrations of T-3 and T-4 in the vanadium-supplemented rats such that they were not different than those of the vanadium-deprived rats whose concentrations were not markedly affected by the increase in dietary iodine. Pancreatic amylase activity was lower in vanadium-supplemented than -deprived rats, and was decreased by luxuriant iodine in vanadium-supplemented diabetes-prone rats and vanadium-deficient diabetes-resistant rats; amylase was not affected by dietary iodine in the vanadium-supplemented diabetes-resistant rats or vanadium-deficient diabetes-prone rats. All of the above information should be useful to other scientists and nutrition specialists providing guidance for intakes of mineral elements.

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0149978 Year: 97 Project Number: 5450-51520-011-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.2.2.2 25%Title: BIOCHEMICAL, PHYSIOLOGICAL, AND NUTRITIONAL ROLES
OF CERTAIN ULTRATRACE ELEMENTS

Period Covered From: 03/96 To: 03/01

Publications:

01. HUNT, C.D. 1996. The biochemical effects of physiological amounts of dietary boron. *J. Trace Elem. Exper. Med.* 9:185-213.
02. HUNT, C.D., HERBEL, J.L. and NIELSEN, F.H. 1997. Metabolic response of postmenopausal women to supplemental dietary boron, magnesium...absorption and retention. *Am. J. Clin. Nutr.* 65:803-813.
03. UTHUS, E.O. and POELLOT, R.A. 1997. Dietary nickel and folic acid interaction to affect folate methionine metabolism in the rat. *Biol. Tr. Elem. Res.* 58:25-33.
04. UTHUS, E.O. 1997. Mathematical modeling of arsenic in hamsters, pp. 176-89. IN: C.O.Abernathy, R.L. Calderon & W.R. Chappell (eds.) *SEGH 2nd Int'l Conf Ar Exp. & Health Eff. Soc. Envi. Geochem. & Health.* Chapman & Hall, London.
05. WIRSAM, B., HAHN, A., UTHUS, E.O. and LEITZMAN, C. 1997. Fuzzy sets and fuzzy decision making in nutrition. *European J. Clin Nutr.* 51:286-296.
06. HUNT, C.D. 1997. Boron and vitamin D deficiencies affect hepatic glycolytic metabolic...chick, pp. 599-601. IN: P.W.F. Fischer et al (ed.) *Proc. Ninth Int. Symp. TEMA*, NRC Research Press, Ottawa, Canada.
07. KEEHR, K.A., IDSO, J.P. and HUNT, C.D. 1997. Effect of marginal and moderate dietary copper deficiency on tibial growth plate morphology in the ...red blood cells. *N.D. Academy of Science Proceedings* 51:204.
08. CRUMMY, L.A., IDSO, J.P., NEWMAN, Jr., S.M. and HUNT, C.D. 1997. Method for preparation of trabecular bone matrix for histological studies using scanning...micsroscopy. *N.D. Academy of Science Proceedings* 51:188.
09. HUNT, C.D., KEEHR, K.A. and IDSO, J.P. 1997. Proximal tibial trabecular bone morphology responds to an interaction amount dietary vitamin D rehabilitation, boron, and...rats. *FASEB J.* 11:A149.

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)

Accession: 0149978 Year: 97 Project Number: 5450-51520-011-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.2.2.2 25%

Title: BIOCHEMICAL, PHYSIOLOGICAL, AND NUTRITIONAL ROLES
OF CERTAIN ULTRATRACE ELEMENTS

Period Covered From: 03/96 To: 03/01

Publications: (Continued)

10. MEACHAM, S.L. and HUNT, C.D. 1997. Estimated cadmium intake of American females. FASEB J. 11:A149.
11. UTHUS, E.O. 1997. Arsenic deprivation decreases the specific activity of betaine homocysteine methyltransferase (BHMT) in rats fed diets low in folic acid but supplemented with choline. FASEB J. 11:A148.
12. NIELSEN, F.H., POELLOT, R.A. and UTHUS, E.O. 1997. Vanadium deprivation alters the changes in plasma thyroid hormone concentrations, pancreatic amylase activity, and serum lactate...dietary iodine. FASEB J. 11:A148.
13. HUNT, C.D. 1997. Regulation of enzymatic activity as a working...animals. Book of Abstracts, 2nd Int. Symp. Health Effects of Boron and its Compounds Univ of California, Irvine, Irvine, CA.
14. MEACHAM, S.L. and HUNT, C.D. 1997. Estimation of US dietary boron consumption. Book of Abstracts, 2nd Int. Symp. on the Health Effects of Boron and its Compounds, Univ. of California, Irvine, Irvine, CA.
15. UTHUS, E.O. 1997. The possible beneficial role of arsenic in methionine metabolism, pp. S22. Arsenic: Health Effects, Mechanisms of Actions and Research Issues, Hunt Valley, MD, Sept 22-24.
16. UTHUS, E.O. 1997. Arsenic essentiality and estimation of a possible requirement, pp. 43. Society of Risk Analysis, Washington, DC. Dec 7-10.
17. WIRSAM, B., UTHUS, E.O., HAHN, A. and LEITZMAN, C. 1997. Application of fuzzy methods for setting RDAs. International Congress of Nutrition, Montreal, Canada, July 27 - Aug 1.
18. NIELSEN, F.H. 1997. Nutritional stressors or arginine and methionine metabolism...response to arsenic deprivation. IN: Arsenic: Health Effects, Mechanisms of Actions & Research Issues, NCI-NIEHS-EPA, Wash DC, abs. S23.

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Title: CENTER DIRECTOR

Date: 01/98

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0149978 Year: 97 Project Number: 5450-51520-011-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.2.2.2 25%Title: BIOCHEMICAL, PHYSIOLOGICAL, AND NUTRITIONAL ROLES
OF CERTAIN ULTRATRACE ELEMENTS

Period Covered From: 03/96 To: 03/01

Publications: (Continued)

19. NIELSEN, F.H. 1997. The nutritional essentiality and physiological metabolism of vanadium in higher animals. IN: Abstract Book, The 5th Chemical Congress of North America, Cancun, Mexico, abs. 35.

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Title: CENTER DIRECTOR

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0146178 Year: 97 Project Number: 5450-51520-011-02 T
Mode Code: 5450-20-00 STP Codes: 5.1.3.4 100% %Title: THE NUTRITIONAL ROLE OF BORON IN THE INHIBITION OF
SERINE PROTEASES

Period Covered From: 01/97 To: 12/97

Progress Report:

Results of studies designed to examine the possible role of dietary boron in the prevention of inflammatory disease suggest that adding amounts of boron typically found in bone tissue enhanced the multiplication of T-cells but not B-cells. Other findings indicated that normal amounts of boron in the diet enhanced the production of antibodies by B-cells. These findings suggest that normal amounts of boron in the diet improve immunity by affecting events early in the immune response process. The above will be of value to scientists and nutrition specialists. This project was inactive from February 28 to December 31, 1997 because of the departure of the research associate assigned to the project. The project will return to active status on February 15, 1998.

Publications:

01. BAI, Y. and HUNT, C.D. 1996. Dietary boron enhances efficacy of cholecalciferol in broiler chicks. *J. Tr. Elel. Exp. Med.* 9:117-132.
02. BAI, Y., HUNT, C.D. and NEWMAN Jr., S.M. 1997. Dietary boron increases serum antibody (IgG and IgM) concentrations in rats immunized with human typhoid vaccine. *N.D. Acad. Sci. Proc.* 51:181.
03. BAI, Y. and HUNT, C.D. 1996. Dietary boron modulates the immune response in the chick. *J. Bone Min. Res.* 11:S320.
04. BAI, Y. and HUNT, C.D. 1997. Boron affects in vitro splenocyte proliferation in a dose dependent manner. *FASEB J.* 11:A148.

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Date: 01/98

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0400356 Year: 97 Project Number: 5450-51530-003-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.3.1.1 25%Title: MINERAL ELEMENTS, PHYSIOLOGICAL FUNCTION &
PERFORMANCE AND BODY COMPOSITION

Period Covered From: 03/96 To: 03/01

Progress Report:

Many physiological functions have been described for magnesium. However, there is a paucity of evidence that dietary magnesium deficiency, independent of concurrent pathology, impairs biological function in humans. Eight postmenopausal women were fed conventional diets containing graded amounts of magnesium to examine the effect of magnesium intake on energy metabolism. When magnesium intake was low (150 mg/d) as compared to the recommended level on intake (350 mg/d), the women used more oxygen, and hence energy, to do the same amount of work on a cycle ergometer. Heart rates during work were increased when magnesium intake was low. Magnesium losses increased (e.g., negative magnesium balance) and skeletal muscle magnesium concentration decreased when magnesium intake was low. These findings indicate that magnesium intake similar to the amount commonly consumed by women in the US results in impaired magnesium metabolism and adversely impacts physiological function. The hypothesis that dietary fat influences iron metabolism indirectly by acting on calcium homeostasis was examined. Weanling male rats were made iron deficient by feeding a diet low in iron (4 mg/kg) for four weeks then were fed diets containing adequate iron (15 mg/kg) and different types of fat (stearate, palmitate, safflower oil, beef tallow) at 20% energy intake. Stearate and palmitate promoted hemoglobin regeneration relative to safflower oil. Total serum and ionized calcium and magnesium, and tibial calcium concentration were not affected by type of dietary fat. These data indicate that dietary fat per se does not adversely impact calcium utilization. Furthermore, the beneficial effects of stearate and palmitate as promoters of iron absorption and utilization are independent of any effects of dietary fat on calcium metabolism. These findings support the hypothesis that specific fatty acids promote iron utilization and provide additional information to augment that stearate and palmitate may be the factor(s) in meat that enhance non-heme iron uptake and utilization. This information will be useful to scientists who prepare recommendations for mineral intakes to promote health and optimal function for the public.

Publications:

01. TURNER, A.A., BOUFFARD, M. and LUKASKI, H.C. 1996. Examination of bioelectrical impedance errors using generalizability theory. Sports Med. Training Rehab. 7:87-103.
02. LUKASKI, H.C. and SMITH, S.M. 1996. Effects of altered vitamin and...cold, pp.1437-56. IN: C.M. Blatteis and J.J. Fregley (eds.), Amer. Physiol. Soc. Handbook of Physiol: Env. Physiol., Vol.2. Oxford Pr., New York, NY.

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Date: 01/98

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ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0400356 Year: 97 Project Number: 5450-51530-003-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 75% 5.3.1.1 25%Title: MINERAL ELEMENTS, PHYSIOLOGICAL FUNCTION &
PERFORMANCE AND BODY COMPOSITION

Period Covered From: 03/96 To: 03/01

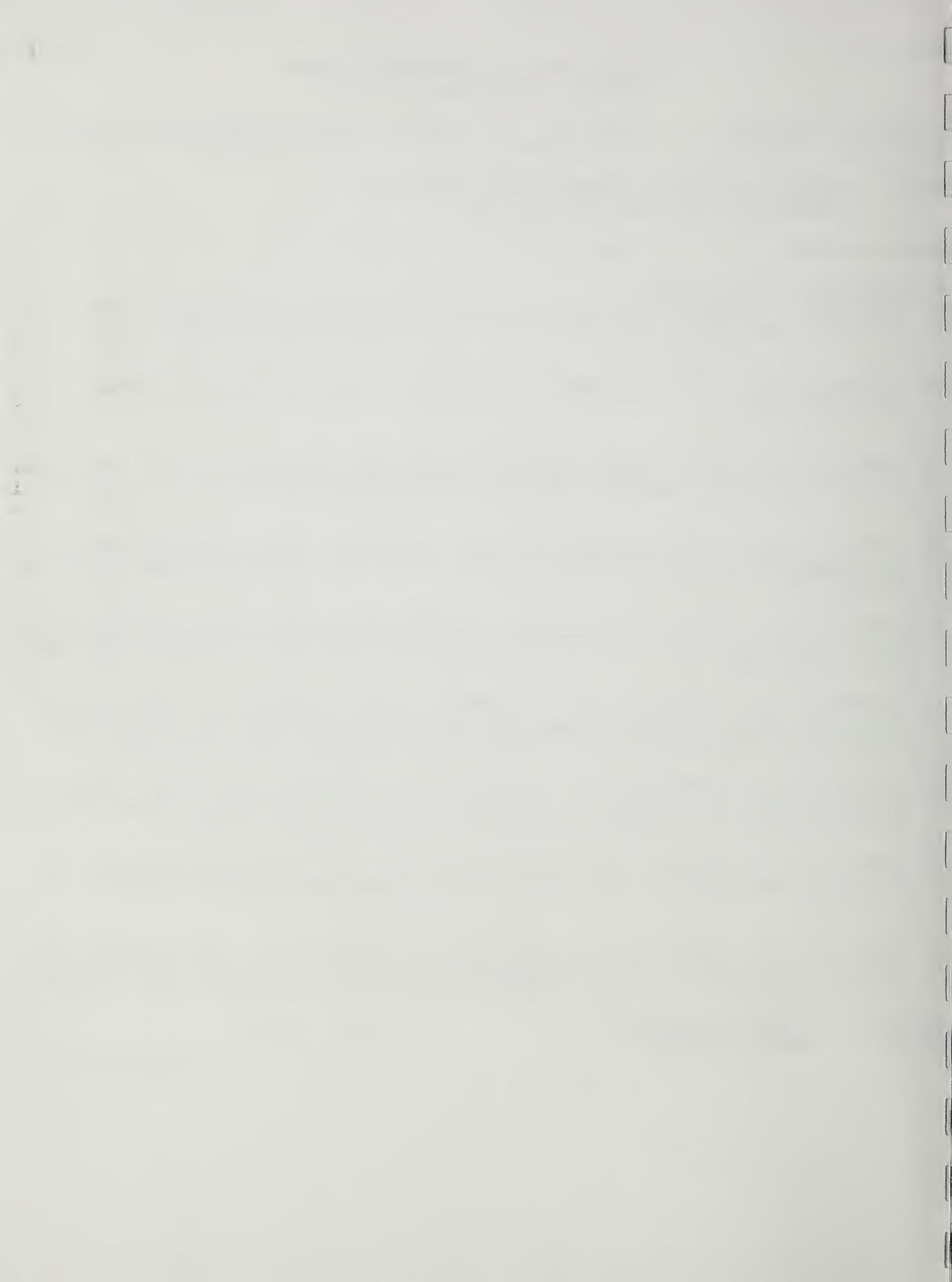
Publications: (Continued)

03. LUKASKI, H.C. 1997. Validation of body composition assessment in the dialysis population. Am. Soc. Artif. Int. Org. J. 43:251-255.
04. LUKASKI, H.C. 1997. Sarcopenia: Assessment of muscle mass. J. Nutr. 127:994S-997S.
05. LUKASKI, H.C. 1997. A new approach to estimate changes in total body water by bioelectrical impedance analysis. Nutrition 13:474-475.
06. LUKASKI, H.C. 1997. Bioimpedance, pp. 1219-1235. IN: R. Dulbecco (ed.), Encyclopedia of Human Biology, 2nd Ed., vol. 10. Academic Press, Inc., San Diego, CA.
07. LUKASKI, H.C. 1997. Body composition in exercise and sport, pp. 621-644. IN: I. Wolinsky (ed.), Nutrition in Exercise and Sport, 3rd Ed. CRC Press, Boca Raton, FL.
08. MCLAREN, C.E., KAMBOUR, E.L., MCLACHLAN, G.J., LUKASKI, H.C. et al. 1996. Multiple linear regression and finite mixture distribution...data. Univ. Queensland (Brisbane, Aus.), Centre for Statistics, Res. Rep. #35.
09. MCLAREN, C.E., KAMBOUR, E.L., HOUWEN, E.L., LUKASKI, H.C. et al. 1996. Patient-specific sequential analysis of hematological data: detection of recovery from iron-deficiency anemia. Blood 88 (Suppl. 1)12b.
10. LUKASKI, H.C., MILNE, D.B. and NIELSEN, F.H. 1997. Work inefficiency in diet-induced magnesium deficiency in postmenopausal women. FASEB J. 11:A147.
11. MCLAREN, C.E., KAMBOUR, E.L., HOUWEN, B., LUKASKI, H.C. and MCLAREN, G.D. 1997. Evaluation of early response to iron replacement in iron-deficiency anemia by patient-specific...hematological data. J. Invest. Med. 45:260A.

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Publications: (Continued)

12. MCLAREN, G.D., LUKASKI, H.C., JOHNSON, P.E., MISEK, A.R. and SMITH, M.H. 1997. Evidence for enhancement of nonheme iron absorption in beagle dogs by typical...tallow, p. 291. Abs. Int. Symp.: Iron in Biol. and Med.
13. SIDERS, W.A. and LUKASKI, H.C. 1997. Comparison of methods of estimating body composition changes during weight loss in women. N.D. Acad. Sci. Proc. 51:220.
14. MICHELSSEN, K.G., HALL, C.B., NEWMAN Jr., S.M. and LUKASKI, H.C. 1997. Copper deficiency and supplementation impact thermoregulation and brown adipose tissue (BAT) mitochondrial...cold. N.D. Acad. Sci. Proc. 51:209.
15. LUKASKI, H.C. 1997. Reply to M.F. McCarty. Am. J. Clin. Nutr. 64:891-892.

Approved: FORREST H NIELSEN
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**INTERIM AND FINAL PROGRESS REPORTS
OF
TERMINATED CRIS WORK UNITS**

ANNUAL RESEARCH PROGRESS REPORT
Report of Progress (AD-421)Accession: 0146625 Year: XX Project Number: 5450-51000-017-00 D
Mode Code: 5450-20-00 STP Codes: 5.1.3.3 100%Title: BIOCHEMICAL CONSEQUENCES OF SUBOPTIMAL DIETARY
INTAKE OF TRACE ELEMENTS

Period Covered From: 04/92 To: 04/97

Progress Report

Zinc (Zn) deficiency in rats reduced the activity of the angiotensin converting enzyme (ACE), the amount of ACE protein and the amount of ACE protein mRNA in testicular germinal cells. These changes also correlated positively with cellular Zn concentration. Other studies disproved the theory that Zn-induced intestinal metallothionein is the mechanism involved in reducing copper (Cu) status in animals fed excess dietary Zn. Studies on diets for laboratory rodents led to the reformulation and publication of new standard rodent diets to replace the previous diets approved by the American Society for Nutritional Sciences. New roles for Cu in signal transduction and the prevention of oxidative damage were discovered. Guanosine triphosphate (GTP), an important molecule for activating signaling pathways, was lowered in platelets of Cu-deficient rats because it was utilized to compensate for impaired mitochondrial energy production caused by reduced cytochrome c oxidase (CCO) activity. Studies showing that platelet CCO activity responded to dietary Cu intakes and correlated positively with liver Cu concentrations indicated that platelet CCO activity is a sensitive index of Cu status in humans. It was also demonstrated for the first time that low Cu intakes could increase oxidative damage to cytoskeletal proteins in red blood cells in rats. This information will be useful to scientists seeking to define human mineral requirements for optimal health and biological function.

Publications:

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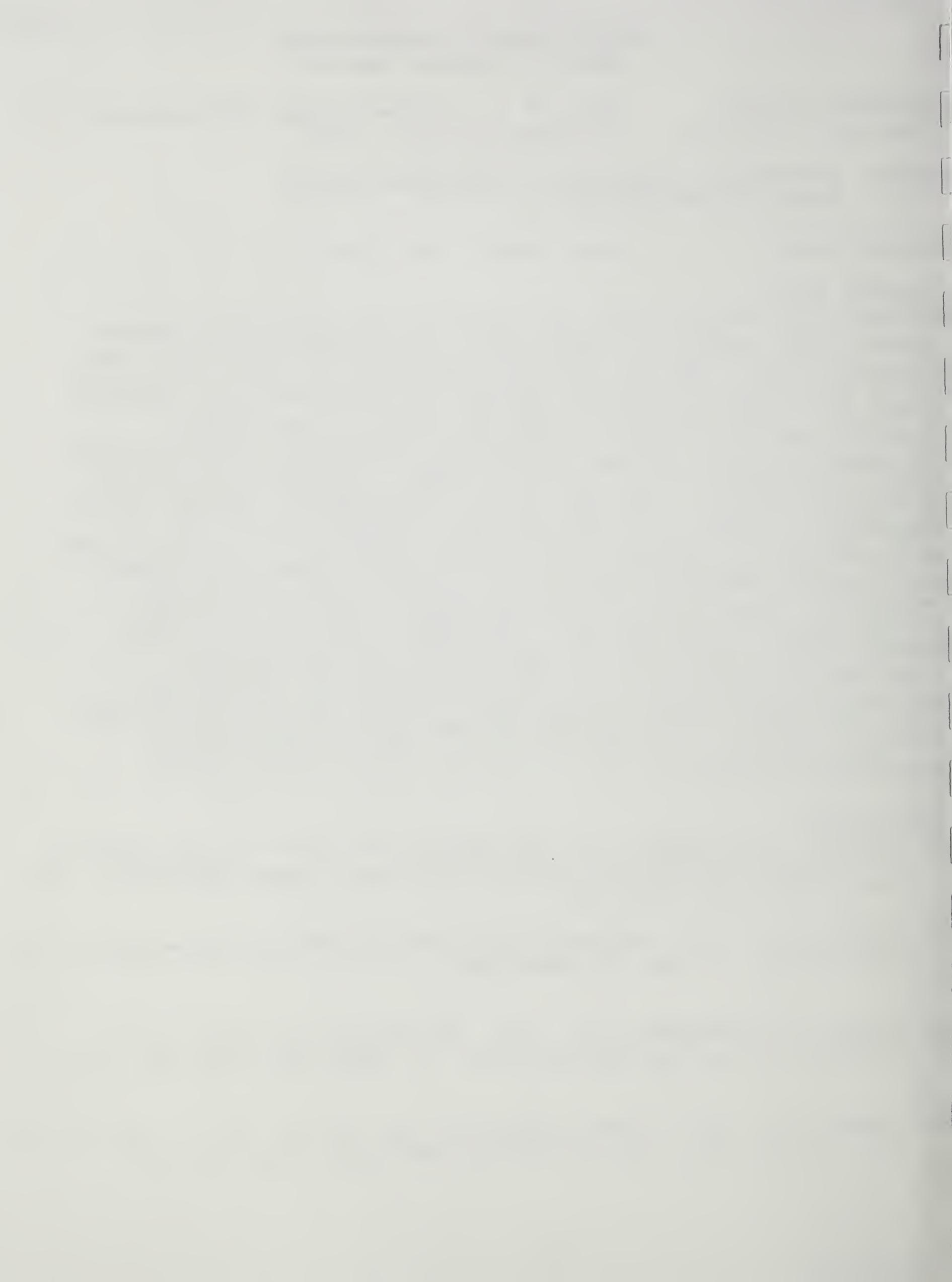
Period Covered From: 01/97 To: 04/97

Progress Report

The effect of maternal copper (Cu) status on the expression of protein kinase C (PKC) isoforms in regions of the developing neonatal brain was examined in rats. Dams were fed diets containing 1, 2, and 6 mg of Cu/kg from 3 weeks prior to conception through the preweaning stage. When the offspring of these dams were 21 days old, specific brain regions (striatum, midbrain, medulla, hypothalamus, hippocampus, cerebral cortex, and cerebellum) were examined for PKC content. Maternal Cu status had differential effects on the expression of immunoreactive isoforms of PKC in the brain regions. PKC alpha content was lowered only in the hippocampus of offspring of dams fed diets containing 1 and 2 mg of Cu/kg, while PKC beta was lowered in the striatum, hypothalamus, and cerebral cortex and PKC gamma was lowered in the striatum, hypothalamus and cerebellum. Because PKC isoforms have specific roles in regulating neuronal growth and development of the central nervous system, these findings indicate that maternal copper deficiency, even marginal deficiency, may adversely affect brain development by impairing the expression of PKC isoforms in regions of the brain that are critical for normal development. These findings will be useful to investigators examining the roles of mineral nutrients in central nervous system development and function.

Publications:

01. SULKASKI, K.A, LABERGE, T.P. and JOHNSON, W.T. 1997. In vivo oxidative modification of erythrocyte membrane proteins in copper deficiency. Free Radic. Biol. Med. 22:835-842.
02. REEVES, P.G. 1997. Components of the AIN-93 diets as improvements in the AIN-76A diet. J. Nutr. 127:838S-841S.
03. REEVES, P.G and NEWMAN, S.M. 1997. Ultrastructural changes in the intestine of rats fed high-zinc diets. J. Trace Elem. Exp. Med. 10:37-46.
04. REEVES, P.G. 1997. Copper, Chapter 13, pp. 175-190. In: I. Wolinski and J.A. Driskell (eds.) Sports Nutrition, CRC Press., Boca Raton, FL.



05. STALLARD, L. and REEVES, P.G. 1997. Zinc Deficiency in Adult Rats Reduces the Relative Abundance of Testis-Specific Angiotensin-Converting Enzyme mRNA. Amer. Soc. for Nutr. Sci., pp. 25-29.

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Publications: (Continued)

06. Momcilovic, B. and Reeves, P.G. 1997. Quantitative Assessment of the Effects of Variability in Dietary Zn Dose-Rate Idiarrhythms Upon Zn.... Using a Slope-Ration Assay. J. Nutr. Biochem. 8:256-264.
07. REEVES, P.G. 1997. Feeding high-zinc diets lowers the copper status in both metallothionein (MT)-null and control mice. FASEB J. 11:A182.
08. JOHNSON, W.T. and THOMAS, A.C. 1997. Evidence of oxidative stress in HL60 cells deprived of copper. FASEB J. 11:A363.

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